UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/489,873	01/20/2000	Gerard Karsenty	9142-006-999	6366

20583 7590 10/22/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
LACOURCIERE, KAREN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/489,873	KARSENTY ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43,44 and 47-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43, 44 and 47-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

Support for the methods of claims 43-60 was not found in the provisional application 60/138,733, therefore, these methods have only been given priority back to the filing date of the instant application, January 20, 2000.

Response to Arguments

Applicant's arguments filed July 31, 2003 have been fully considered but they are not persuasive. Applicant argues that the provisional application 60/138,733 does provide support for the instantly claimed methods of determining modulators of bone formation because the Application describes methods of treating bone disease by modulating leptin concentrations, assays to determine bone mass and leptin concentrations and points to particular passages of the provisional to support this assertion. This is not persuasive because the claimed methods are not drawn to methods of treating bone disease by modulating leptin concentrations, assays to determine bone mass and leptin concentrations, but rather to methods of identifying compounds to be tested for an ability to modulate bone mass and methods wherein such compounds are tested for the ability to modulate bone mass in a mammal. No support could be found for these methods in the provisional application, including at the passages cited by Applicant, for example, page 2, line 21 to page 3, line 19 are directed entirely to disease treatments and Examples 2-5 do not teach methods of screening, as claimed. The claimed methods have only been given priority to the instant filing date.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43, 44, and 47-60 are maintained as rejected and new claims 61 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ke et al. (US Patent No. 6,352,970) in view of Tartaglia et al. (US Patent No. 6,403,552), Freidman et al. (US Patent No. 5,935,810, reference AB cited on PTO form 1449, filed Feb. 6, 2001) and Simonet et al. (reference BS cited on PTO form 1449, filed Feb 6, 2001).

Claims 43, 44 and 47-62 are drawn to methods of identifying compounds to be tested for an ability to modulate bone mass and methods wherein such compounds are tested for the ability to modulate bone mass in a mammal. The methods of identifying compounds to be tested include determining whether a compound binds to a leptin

polypeptide or leptin receptor polypeptide, determining whether a compound alters the level of leptin/leptin receptor complexes and contacting a cell expressing a leptin receptor with the compound alone or in combination with leptin and determining if the compound increases or decreases the activation of the leptin receptor. Specifically claimed are methods wherein the determinination of the level of activation of the leptin receptor is performed by measuring levels of phosphorylated Stat3 polypeptide. The methods of identifying a compound that modulates bone mass in a mammal include the additional step of administering the compounds identified by these methods to a non-human mammal and determining whether the bone mass is modulated relative to an untreated control animal.

Ke et al. teach leptin as a regulator of bone formation and teach using leptin or a leptin mimetic to treat diseases associated with decreased bone mass. Ke et al. teach assays to determine bone mass in mammals in vivo. Ke et al. do not teach assays to identify compounds to be tested for an ability to modulate bone mass. Ke et al. do not teach assays wherein leptin/leptin receptor complexes are measured. Ke et al. do not teach assays wherein a cell expressing the leptin receptor is used to assay for compounds, nor do Ke et al. teach measuring levels of Stat3 phosphorylation to determine leptin receptor activation. Ke et al. do not teach regulating leptin levels as a means to treat conditions associated with increased bone mass.

Tartaglia et al. teach assays to determine modulators of leptin receptor (using the name Ob receptor (ObR), as taught by the specification as an alternative name for leptin receptor), including assays wherein a compound is assayed for its ability to bind

to leptin receptor, leptin/leptin receptor complexes are measured in the presence and absence of compounds and a cell expressing leptin receptor is contacted with a compound and the level of expression is measured. Tartaglia et al. teach using compounds identified in these methods in non-human mammals in assays to determine if they regulate levels of leptin receptors in vivo. Tartaglia teach these assays wherein the level of phosphorylation of a Stat protein is measured, including Stat3 (see for example column 71). Tartaglia et al. do not teach their methods for use in determining modulators of bone mass, nor do they teach methods of measuring bone mass.

Friedman et al. (US Patent No. 5,935,810, reference AB cited on PTO form 1449, filed Feb. 6, 2001) teach assays for screening for substances that are potentially modulators of leptin in mammals (see for example, column 6).

Simonet et al. (reference BS cited on PTO form 1449, filed Feb 6, 2001) teach diseases that are associated with increased bone density.

At the time the instant invention was made, it would have been obvious to determine compounds to be tested for their ability to modulate bone mass in a mammal, and subsequently test these compounds for their ability to modulate bone mass in a non-human mammal, because Ke et al. teach that leptin modulates bone mass and compounds which modulate leptin and the leptin receptor are useful for treating conditions wherein bone mass is lowered. It would have been obvious to determine compounds to be tested, and subsequently test these compounds in mammals, including performing assays wherein compounds that bind leptin or the leptin receptor are determined, assays wherein leptin/leptin receptor complexes are measured, assays

wherein activated Stat3 levels are determined and assays wherein a cell expressing leptin receptor is used because the prior art taught these methods for use in determining potential modulators of leptin and leptin receptor (see, for example, Tartaglia et al. and Friedman et al.). Tartaglia et al. and Friedman et al. teach their assays for use in determining leptin and leptin receptor modulators because of the role of leptin in obesity; however, it would have been obvious to use these methods to determine modulators of leptin and leptin receptor for any purpose. Tartaglia et al. and Friedman et al. teach the next step as testing potential modulators in vivo in non-human animals, and it would have been obvious to do the same with compounds tested for the potential to modulate bone mass because Ke et al. teach assays to test for bone mass modulation in vivo and it would be an obvious step once a potential drug had been determined. It would have been obvious to test for compounds that increase or decrease bone mass because Ke et al. teach leptin as a regulator of bone mass and the prior art recognized medical conditions associated with both increased and decreased bone mass (see, for example, Simonet et al.). One of ordinary skill in the art would have been motivated to practice methods of determining compounds to be tested for their ability to modulate bone mass, and subsequently test such compounds in non-human mammals because Ke et al. teach such compounds are useful for treating bone diseases. One skilled in the art would have been motivated to practice these methods by determining compounds that bind to leptin or leptin receptor, by assays wherein a compound is assayed for its ability to bind to leptin receptor, leptin/leptin receptor complexes are measured in the presence and absence of compounds and a cell

expressing leptin receptor is contacted with a compound and the level of expression is measured because these assays were known in the prior art for determining modulators of leptin and leptin receptor.

Therefore, at the time the instant invention was made, the invention of claims 43, 44 and 47-60 would have been obvious to one of ordinary skill in the art, as a whole, based on the teachings of Ke et al., Tartaglia et al., Freidman et al. and Simonet et al.

Response to Arguments

Applicant's arguments filed July 31, 2003 have been fully considered but they are not persuasive.

In response to the rejection of record under 35 USC 103(a) as being unpatentable over Ke et al. (US Patent No. 6,352,970) in view of Tartaglia et al. (US Patent No. 6,403,552), Freidman et al. (US Patent No. 5,935,810, reference AB cited on PTO form 1449, filed Feb. 6, 2001) and Simonet et al. (reference BS cited on PTO form 1449, filed Feb 6, 2001), Applicant argues that the references cited do not teach all of the limitations of the claimed invention, specifically, that the primary reference, '970, does not teach or suggest that activation of the leptin receptor mediated by leptin/leptin receptor complex formation results in decreased bone mass and actually teaches away from the claimed invention because '970 teaches that in a cascade, leptin/leptin receptor complex formation eventually causes increased bone mass.

These arguments have been fully considered, but not found to be persuasive. To begin with, Applicant states that all claims are now drawn to methods wherein the

compound decreases bone mass, however, newly submitted claim 61 and 62 are drawn to methods wherein the compound increases bone mass. Further, the claimed methods are drawn to methods of determining compounds that modulate bone mass, wherein the compounds increases or decrease bone mass. Although '970 teaches a compound that eventually causes an increase in bone mass, the cited references also teaches bone conditions known to require treatment that would decrease bone mass. Given that '970 clearly teaches a role for the leptin/leptin receptor complex in bone mass formation, the skilled artisan would be motivated to search for regulators of the leptin/leptin receptor complex for either purpose, given that the art recognized a need to increase or decrease bone mass. Further, methods of screening, as claimed, are obvious and would be expected to provide compounds that up or down regulate bone formation through that screening process.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Thursday 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
October 20, 2003

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER